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Subject review

Development of Additive Manufacturing in the Medical Field: a review

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Abstract: Additive manufacturing has become widely used in various industries because of technological advancements. Among these industries, the healthcare sector has emerged as one of the most promising areas for the application of AM technologies. In the healthcare sector, AM offers substantial benefits by delivering customized solutions for patients. Today, with the growing diversity of materials and the evolution of additive manufacturing techniques, treatment procedures are implemented by modeling tissues and organs based on patient anatomy. Additionally, the creation of customized implants and medical devices for different treatments can also be accomplished. In implant production, designs are created to ensure optimal osseointegration. In the future, additive manufacturing aims to minimize the need for organ donations by advancing four-dimensional printing technology, which incorporates the concept of time into three-dimensional printing, allowing for the creation of customized artificial organs. This review explores the materials, manufacturing techniques, and applications frequently utilized in AM within the medical sector.

Keywords: additive manufacturing; biomaterials; bioprinting; three-dimensional printing

1 INTRODUCTION

Additive manufacturing (AM), also referred to as three-dimensional (3D) printing, encompasses a set of production technologies that have evolved from the late 1980s to the present. [1]. According to the American Society for Testing and Materials (ASTM) standard F2792-10, AM is defined as "a process of joining materials to make objects from 3D model data, usually layer upon layer, as opposed to subtractive manufacturing methodologies" [2]. AM technology has been under development for more than 40 years and has attained a level of maturity that allows for its commercial application across various industries, such as automotive, aerospace, consumer products, and biomedical engineering. [3, 4]. As substances like advanced metals [5], ceramics [6], polymers [7], and hydrogels [8] continue to advance quickly, the scope of applications for AM widens. Furthermore, progress in machine technologies, such as multi-color and multi-material printing, boosts the potential of this constantly evolving manufacturing process [9]. According to International Standart of Organization and ASTM standardizations, AM processes are categorized into seven distinct types, as shown in Fig. 1: "Material Extrusion (ME), Powder Bed Fusion (PBF), Material Jetting (MJ), Photopolymerization (P), Binder Jetting (BJ), Directed Energy Deposition (DED), and Laminated Object Manufacturing (LOM)". The types of PBF processes include Selective Laser Sintering (SLS), Selective Laser Melting (SLM), Direct Metal Laser Sintering (DMLS), and Electron Beam Melting (EBM). Additionally, P includes techniques such as Stereolithography (SLA) and Direct Light Processing (DLP) [10].

AM relies on 3D model data and continuous additive fabrication technologies [11]. Unlike conventional manufacturing methods, AM can create intricate 3D structures directly in a single piece with increased production precision, streamlined manufacturing procedures, efficient material usage, reduced processing time, and enhanced processing efficiency. Additionally, it can be applied in various medical fields to fulfill customized requirements [11-14]. The structure of living tissues and organs can be produced using suitable AM methods by selecting materials that provide the necessary flexibility and durability [15]. 3D printed tissue and organ models are also used for purposes such as surgical preparation and medical training [16]. The manufacturing of implants involves modifying the porosity of the components to more closely align with bone characteristics, ensuring compatibility with bone implants [17]. Patient-specific implants and medical devices contribute to higher success rates in treatment processes [15-17].

This study emphasizes the materials used in AM technology within the medical sector, the AM methods, and developments in different medical application areas. The uses of AM in the medical field are analyzed under two primary categories: "tissue and organ applications" and "implant and medical device applications."

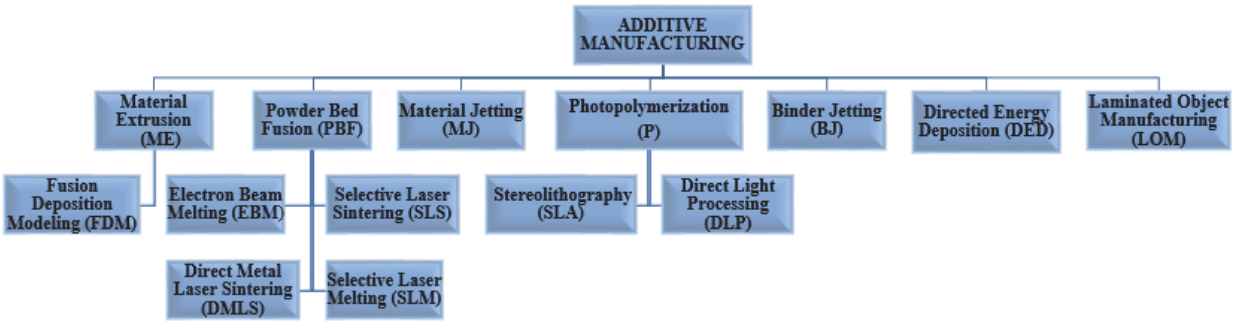

Figure 1 Additive manufacturing process types

2 MATERIALS UTILIZED IN ADDITIVE MANUFACTURING FOR THE MEDICAL FIELD

A diverse range of materials is accessible for various AM techniques. In the medical sector, products must be made from materials that are biocompatible, meaning they do not harm human health. These materials are referred to as biomaterials. A biomaterial is described as a natural or synthetic material or a composition of materials used for a specific duration as part or all of a system that replaces, cares, or improves any organ, tissue, or body function [18, 19]. In the medical domain, biomaterials must demonstrate excellent biological compatibility with living cells, be easily manufacturable, have high durability, and possess good flexibility [20, 21]. Biocompatibility refers to the ideal compatibility of a biomaterial with body tissues concerning its physical, chemical, biological characteristics, and the mechanical behavior of the body [22].

In AM techniques, materials used for medical applications are categorized into metals, ceramics, polymers, and hydrogels. Tab. 1 shows the applications and the AM production techniques used according to different types of biomaterials.

Table 1 Additive manufacturing production methods for medical applications by material type

Material Type	Example Materials	Applications	Additive Manufacturing Technique	Ref.
Metal	Titanium and alloys, stainless steel, magnesium, tantalum, nickel, aluminum, cobalt-chromium alloys, nickel-titanium	Orthopedic implants, dental implants, heart valves, pacemakers, stents,orthodontic devices, bone screws	SLM, SLS, EBM	[25, 36, 38, 39, 40]
Ceramic	Zirconia, alumina, bioactive glasses, diamond-like carbon	Dental crowns, dental implants, dental prostheses, joint surface coatings, knee prostheses, spinal implants	FDM, DLP, SLS, Inkjet printing	[45-47, 50]
Polymer	Polyether ether ketone, polylactic acid, polycaprolactone, polyvinyl alcohol, polyurethane	Prosthetics, medical devices, tissue engineering scaffolds, orthopedic implants, tissue and organ modeling, plates, surgical guides, drug-delivery tools	SLA, FDM, Inkjet printing, Extrusion	[56-59]
Hydrogel	Natural and synthetic composites, hyaluronic acid, Gelatin methacryloyl, alginate, polyethylene glycol, methacrylated hyaluronic acid	Tissue engineering scaffolds, cell-loaded scaffolds, drug delivery systems, biosensors	SLA, FDM, DLP, Inkjet printing, Extrusion	[61, 64, 65, 67, 69]

2.1 Metals

Metal-based components intended for biomedical purposes are required to exhibit high mechanical performance, resistance to corrosion, and exceptional biocompatibility [23]. Biocompatibility, in this context, refers to a material's ability to perform its function without inducing adverse local or systemic reactions within the surrounding tissues. Commonly preferred metallic biomaterials include titanium (Ti) and its alloys, stainless steel (SS), and cobalt-chromium (Co-Cr) alloys due to their well-established compatibility with biological environments [24]. Ti and its derivatives are especially favored in medical device production, owing to their reliable long-term behavior under physiological conditions [25]. These materials are characterized by low density, elevated tensile strength, and excellent biocompatibility. As a result, they are utilized in a wide range of medical applications such as orthopedic implants, joint replacements, and prosthetic heart valves [26]. Furthermore, Ti-based materials are widely employed in dental implants [27] and maxillofacial reconstructive surgeries [28]. The incorporation of periodic lattice geometries within Ti structures has been shown to enhance mechanical stability and improve osseointegration [29].

SS grades such as 316 and 316L, which contain chromium, nickel, and molybdenum, are commonly applied in mandibular reconstructions due to their corrosion resistance [30, 31]. However, these steels are generally not recommended for permanent implants due to their relatively poor mechanical strength [32]. This limitation has prompted the use of alternative metals for structural applications. Co-Cr alloys, known for their high hardness, wear resistance, and favorable biocompatibility, are extensively used in dental restorations [33, 34]. They also exhibit outstanding resistance to corrosion in physiological fluids, making them ideal for load-bearing implants [35]. Tantalum, another biocompatible metal, has gained popularity in high-end implant applications due to its ability to promote bone ingrowth [36]. Despite its excellent chemical inertness, its clinical usage remains limited by complex manufacturing processes and elevated production costs [37]. In addition to these, magnesium-based materials are gaining prominence for their biodegradability and compatibility in temporary implant applications, particularly where gradual resorption is desired [38]. Among shape memory alloys, nickel-titanium (NiTi) stands out for its high elasticity, strength, and biological compatibility [39]. NiTi is used in various medical applications such as stents, orthodontic devices, and kidney stone retrieval tools, and it is often processed via AM techniques like SLM [40]. With the advancement of AM, especially PBF based methods, it has become possible to fabricate intricate metallic medical structures with controlled porosity and tailored mechanical behavior. Techniques such as SLM, SLS, and EBM solidify metal powders layer-by-layer to produce customized implants [41]. Porous structures created using these technologies not only allow for elastic modulus matching with native bone [42] but also facilitate bone cell proliferation and stable implant fixation [43].

2.2 Ceramics

Bioceramics are a class of ceramic materials specifically engineered to restore or replace

malfunctioning biological structures [44]. These materials are broadly divided into two primary categories based on their interaction with body tissues: bioinert ceramics and bioactive glasses. While bioinert ceramics tend to resist interaction with surrounding tissue, bioactive variants can chemically bond with bone or soft tissue, enhancing implant integration.

Oxide-based bioinert ceramics, including alumina and zirconia, are frequently employed in medical applications such as dental implants, bridges, crowns, and hip joint prostheses. Zirconia implants, in particular, have demonstrated encouraging osseointegration behavior, which plays a crucial role in their increasing clinical adoption [45]. Additionally, zirconia-based components have been successfully processed using SLS technology for various dental and orthopedic applications [46]. On the other hand, non-oxide ceramics, such as carbon-based materials like diamond-like coatings, are typically used for heart valves, joint surface coatings, knee prostheses, spinal implants, and certain dental devices [47].

Bioactive glasses, composed primarily of silica, were the first known ceramic-based materials capable of forming direct bonds with both soft and hard tissues in vivo [48]. This unique capacity for biological interaction has led to their widespread exploration in bone regeneration and tissue engineering.

With the rapid progress in AM, bioceramic components can now be fabricated using several advanced methods, including SLA, DLP, fused deposition modeling (FDM), SLS, SLM, and inkjet printing [49]. Advancements in ceramic printing have enabled the creation of high-precision, biocompatible structures using DLP and SLS methods, overcoming many of the geometric and material limitations of traditional processing [50]. These AM technologies allow for the fabrication of porous or customized geometries that better match the mechanical and biological properties of native tissue.

2.3 Polymers

Polymers have emerged as the primary printing material in the realm of 3D printing. In medical applications, polyether ether ketone (PEEK), polylactic acid (PLA), and polycaprolactone (PCL), are prevalent materials for 3D printing [51]. PLA is an eco-friendly material with excellent biodegradability and is used in dentistry, surgical modeling, and bone scaffolding applications.

PCL is a material with superior properties for creating tracheal stents and soft tissue applications. PEEK has an elastic modulus comparable to that of human bones [51-53]. PEEK is also used in the production of prosthetic parts, spinal, and orthopedic implants [54].

Structures made of polymer materials are commonly produced using AM methods like SLA and FDM [52, 53, 55].

Polymers have become one of the most versatile and widely used material groups in AM, particularly in the field of 3D printing. In biomedical applications, PEEK, PLA, and PCL stand out as frequently utilized thermoplastics due to their biocompatibility, processability, and functional adaptability [51]. PLA is a biodegradable, environmentally friendly polymer often used in dentistry, surgical models, and bone scaffold structures. Additionally, polymer-based anatomical models allow for advanced preoperative planning and simulation in complex surgeries, enhancing clinical precision [56].

PCL exhibits favorable characteristics for soft tissue engineering, especially in applications such as tracheal stents, due to its flexibility and slow degradation rate. Scaffolds fabricated using PLA and PCL have demonstrated excellent support for tissue regeneration in vitro, further supporting their potential in regenerative medicine [57]. On the other hand, PEEK offers a high-performance alternative with an elastic modulus that closely approximates that of natural bone, making it particularly suitable for load-bearing implants [51-53]. It is commonly employed in the fabrication of spinal devices, orthopedic implants, and prosthetic components [54]. Furthermore, PEEK and PLA have been widely used in prosthetics and orthotic devices due to their customizable mechanical properties, which can be tailored to meet individual patient needs [58]. Other polymers, such as polyvinyl alcohol and polyurethane, are also used for temporary support structures and soft-tissue modeling, expanding the applicability of AM in complex biomedical applications [58, 59].

Beyond structural applications, the chemical versatility of polymers enables their use in developing functional medical devices. 3D printed drug-delivery medical tools are often designed using polymers due to their chemical flexibility, allowing for targeted release and biocompatibility [59]. To manufacture such polymer-based structures, AM techniques such as SLA and FDM are frequently utilized [52, 53, 55]. These methods allow for the creation of intricate geometries and patient-specific devices with relatively low production costs and high precision.

2.4 Hydrogels

Hydrogels are 3D, hydrophilic polymer networks characterized by their high water content and soft, tissue-like mechanical behavior. These features make them exceptionally well-suited for use in bioprinting technologies. Because of their excellent biocompatibility, minimal immunogenic response, and tunable mechanical and chemical properties, they have been extensively explored and optimized for applications in tissue engineering [60]. They can be engineered to mimic the extracellular matrix (ECM), providing an ideal microenvironment for cell adhesion, proliferation, and differentiation [61].

One of the most widely investigated hydrogel materials is gelatin methacryloyl (GelMA), which can be crosslinked through photopolymerization to fabricate cell-laden constructs with tailored geometries [62, 63]. This material allows for the creation of vascularized and architecturally complex tissue scaffolds, enhancing its relevance in regenerative therapies. Similarly, methacrylated hyaluronic acid (HAMA) has gained prominence in bioprinting due to its inherent role in the native ECM and has been applied in fabricating scaffolds embedded with viable cells for cartilage and soft tissue regeneration [64].

Recent developments have also introduced stereolithographic 3D printing as a method for producing drug-loaded hydrogel systems, offering controlled drug release profiles within personalized geometries [65]. Hydrogels find broad applications including but not limited to cell-laden scaffolds [64], bioinks for tissue engineering [61, 66], synthetic ECM formulations [67], regenerative medicine platforms [68], and biosensing devices [69]. Examples of hydrogel systems under investigation include polyethylene glycol (PEG) based hydrogels for cartilage repair, alginate-based hydrogels for islet cell transplantation, and HAMA-GelMA composites for osteochondral defect regeneration [61,64].

3 ADDITIVE MANUFACTURING TECHNOLOGIES IN THE MEDICAL FIELD

AM technologies offer a broad spectrum of techniques tailored to the requirements of biomedical applications. These technologies are selected based on material compatibility (e.g., metal, polymer, ceramic, hydrogel), structural precision, biological function, and the targeted clinical application. In particular, bioprinting methods are essential for fabricating tissue-engineered constructs and implantable devices where cellular integration is required [70]. The unique feature distinguishing bioprinting from conventional AM methods is the incorporation of living cells and bioactive agents into hydrogels (bioinks), enabling the development of biologically functional 3D structures [71]. Common bioprinting strategies include inkjet, extrusion-based, and laser-assisted approaches [72].

The most frequently utilized AM technologies in the medical field are FDM, extrusion-based printing/bioprinting, PBF, SLA, and inkjet/BJ [73]. Each of these technologies serves a unique purpose depending on the material used and the functional or structural requirement of the medical application.

3.1 Fused Deposition Modeling

FDM is one of the most widely adopted AM techniques in the medical field due to its accessibility, cost-effectiveness, and compatibility with biocompatible thermoplastic materials [74]. FDM involves extruding and immediately solidifying a molten thermoplastic material. Filaments are melted in the nozzle by a transfer system, then extruded from the nozzle, solidified, and finally built layer by layer [75]. Some commonly utilized printing filaments include PLA, nylon, polycarbonate, and polyvinyl alcohol (PVA). Lactic acid-based polymers, such as PLA and PCL, are renowned for their biocompatibility and biodegradability, making them extensively used in medical applications [76]. PLA and PCL are particularly suited for biodegradable implants and bone scaffolds, while PVA is often used for water-soluble supports and anatomical models.

FDM is frequently used in the fabrication of anatomical models for surgical simulations, dental guides, customized prosthetics, and orthotic devices. In tissue engineering, FDM enables the production of porous polymer-based scaffolds with tailored geometrical and mechanical properties [76].

3.2 Extrusion-Based Bioprinting

Extrusion-based bioprinting is a predominant technology used to fabricate tissue constructs by extruding cell-laden hydrogels (bioinks) through a nozzle using pneumatic, piston, or screw-driven forces [77]. This technique is particularly well-suited for printing shear-thinning hydrogels that maintain their shape upon deposition. Frequently used materials include natural polymers such as Gel, alginate, HA, and collagen, as well as synthetic ones like PEG and PVA [78-82].

Applications of extrusion bioprinting encompass cartilage regeneration [80], bone scaffolds [83], vascularized grafts [84], and engineered skeletal muscle [85]. Thermo-sensitive and photo-crosslinkable hydrogels such as GelMA and HAMA provide structural integrity and tunable mechanical properties. Multi-nozzle printing systems enable the spatial distribution of multiple cell types and biochemical signals within the same construct, facilitating tissue heterogeneity and function [79].

3.3 Powder Bed Fusion

PBF encompasses techniques like SLS, SLM, and EBM, each suited to different material types and functional demands [86].

SLS is commonly employed for polymeric and ceramic powders, such as nylon and zirconia, to produce dental restorations, anatomical guides, and surgical tools [87, 88]. It enables high-resolution parts without requiring support structures, making it suitable for intricate geometries[89, 90].

SLM is used for fabricating fully dense metallic parts from materials like Ti alloys, Co-Cr, SS, and NiTi, which are extensively used in orthopedic, spinal, and dental implants [91, 92]. These implants often feature lattice or trabecular structures that promote osseointegration and load distribution [93, 94].

EBM operates in a vacuum environment and utilizes electron beams to fuse metal powders, especially Ti6Al4V alloys, with lower residual stress and excellent fatigue properties. It is ideal for manufacturing large, porous orthopedic structures such as femoral stems, acetabular cups, and cranial plates [92].

3.4 Stereolithography

SLA is a vat photopolymerization technique that uses ultraviolet or visible light to cure liquid photopolymers into solid objects layer-by-layer with high precision [95]. It is particularly suitable for fabricating highly detailed models, microfluidic devices, and biomedical components requiring smooth surface finishes and complex geometries.

SLA compatible materials include photoreactive polymers and hydrogels such as PEG-diacrylate, GelMA, and HAMA. While SLA parts typically lack the mechanical strength of sintered or extruded components, they are ideal for visual modeling, dental molds, hearing aids, and organonachip platforms [96, 97]. Advances in SLA include integrating bioinks for cellular constructs and improving cytocompatibility through refined resin chemistries [95].

3.5 Inkjet/Binder Jetting

Inkjet and BJ are non-contact, droplet-based techniques that allow precise placement of bioinks or binders to build structures layer-by-layer [98]. Inkjet bioprinting employs piezoelectric or thermal actuation to deposit hydrogels such as alginate, PEG, and Gel that may contain live cells or biological factors [72, 88].

This method is used to fabricate soft tissue models, skin grafts, and vascular constructs with precise control over spatial resolution. Multimaterial inkjet systems facilitate localized delivery of signaling molecules and heterocellular arrangements.

BJ differs by selectively applying a binder (e.g., phosphoric acid or aqueous PVA solution) to a powder bed of materials such as hydroxyapatite or tricalcium phosphate, forming porous scaffolds suitable for bone tissue engineering [99]. BJ has also been explored for printing drug-loaded tablets and patient-specific pharmaceutical formulations [90, 97]. Continued advancements in droplet control, printhead precision, and bioink formulations are enhancing the versatility and reproducibility of inkjet and binder-based systems in personalized medicine.

4 APPLICATIONS OF ADDITIVE MANUFACTURING IN THE MEDICAL FIELD

AM technologies have revolutionized the production of medical components by enabling the development of complex, customized structures that were previously difficult to fabricate with traditional methods. These technologies allow for the design and manufacture of patient-specific medical solutions with high precision, reducing production time and cost while improving treatment outcomes. In recent years, 3D printing has been increasingly applied in diverse healthcare areas, such as tissue engineering, implant development, prosthetics, surgical planning, and the fabrication of medical devices [100, 101, 102]. The flexibility in design and material selection offered by AM techniques makes them highly suitable for addressing the anatomical and functional needs of individual patients [103]. In this context, a wide variety of materials including polymers, ceramics, metals, and composites have been utilized to create medical products tailored to specific clinical requirements [104, 105]. Moreover, AM has facilitated the advancement of personalized medicine by enabling the fabrication of biologically compatible structures that can promote cell growth and tissue regeneration [106, 107]. The following sections provide a comprehensive overview of key applications of AM in the medical field, with particular focus on tissue/organ regeneration and implantable device production.

4.1 Tissue and Organ Applications

Tissue engineering seeks to create techniques that facilitate the repair and reconstruction of injured tissues and organs through the combination of elements such as medicine, biology, material structure, and material mechanics. Such tissue and organ damage often involves critical defects in bone, skin, or nerve tissue caused by various traumas and tumors. The structures used in tissue engineering applications must fulfill many functions of living tissue. Therefore, these structures are produced using various 3D bioprinting methods. To ensure the homogeneous distribution of cells at the damaged site and to enable the regenerated tissue to perform its metabolic and mechanical functions, scaffolds featuring a porous architecture are produced. The porous structures for the regenerated tissue are first cultured in vitro using bioink for cell seeding, and subsequently, the partially regenerated tissue is inserted into the damaged area. When tissue damage is fully regenerated, biodegradable materials such as polymers or hydrogels composed of various polymers are commonly used to ensure the complete absorption of the implanted scaffold [104]. Additionally, ceramic materials can be combined with polymers to create composite materials, which are used for tissue engineering scaffolds to provide mechanical strength and good biocompatibility [105].

3D bioprinting technique has been applied in the creation of biological tissues in different fields, such as heart valves, skin, bone, cartilage, and kidneys [84, 100, 106-108]. Mota and colleagues [100] successfully implemented a tissue regeneration method in a patient's mandibular tissue. Fig. 2 schematically shows the process steps of the production and regeneration of mandibular tissue using 3D bioprinting. The process begins with data collection through medical imaging. A 3D solid model of the damaged tissue and a suitable scaffold is created. A porous scaffold structure is then produced using AM technology. Afterward, the scaffold is subjected to appropriate cell seeding and cultured to reach the necessary tissue level. Finally, the scaffold is implanted, leading to tissue regeneration.

Duan et al. [84] utilized an extrusion-based 3D bioprinting technique to produce heterogeneous aortic valves using alginate/gelatinhydrogels. Encapsulated smooth muscle cells and valvular interstitial cells were observed to possess superior properties in culture, including high viability, good spread, and preservation of phenotype. Therefore, it was determined that 3D bioprinted cell-encapsulated valves produced in tissue engineering are a suitable method for heart valve replacements.

Kankala et al. [106] employed 3D printing technology with different composites to create scaffolds with properties similar to natural bone tissue. 3D porous scaffold structures were produced using Gel, nano-hydroxyapatite (n-HA), and poly(lactic-co-glycolic) (PLGA) inks and tested experimentally. The produced Gel/n-HA/PLGA scaffold structures demonstrated strong hydrophilicity, outstanding biocompatibility, and osteogenic properties, with no toxic substances detected during the degradation process. Furthermore, it was observed that they effectively supported the proper adhesion of osteoblasts, as well as their growth, differentiation, and proliferation.

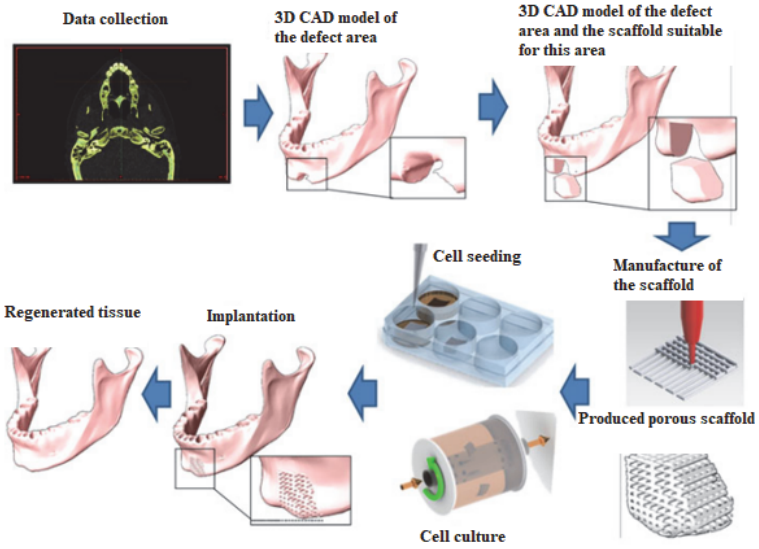

Figure 2 Production and renewal process of mandibular tissue using 3D bioprinting [100]

Kundu et al. [107] used various PCL and chondrocyte cell-encapsulated alginate hydrogels to produce 3D cell-printed scaffolds for cartilage tissue formation using the AM method. Among the various PCL and alginate hydrogel structures, it was found that PCL-alginate hydrogels containing transforming growth factor-β exhibited better self-tissue merging and ECM formation performance. The created 3D cell-printed scaffolds were implanted into mouse subcutaneous tissue, and histochemical analyses were performed after one month. As a result of these analyses, an increase in type II collagen fibril formation and cartilage tissues was observed.

Lawlor et al. [108] produced human kidney organoids using extrusion-based 3D bioprinting. The production method used allowed for accurate regulation of organoid size, cell count, and structure. The in vitro experimental model of kidney organoids produced with various enhancements can be utilized for pharmaceutical testing or disease simulation.

In tissue and organ applications, beyond the creation and repair of living tissues, 3D printing technologies are also applied in surgical modeling. These personalized tissues and organs provide surgeons with the opportunity to perform preoperative surgical planning.

Figure 3 (A) A preoperative 3D printed liver and the recipient's actual liver. The long arrows indicate the hepatic artery, the short arrows indicate the hepatic vein, and the double arrows indicate the portal vein. (B) A preoperative 3D printed right lobe and the donor's actual right lobe. The single arrows indicate the hepatic artery, and the double arrows indicate the portal vein [109]

Zein et al.[109] produced synthetic liver structures, including complex vascular and biliary architectures, using SLA technology (Fig. 3). In this study conducted for preoperative planning purposes, liver models of three donors and three recipients were examined. No new complications were encountered during surgeries, and operation times were reduced.

4.2 Implant and Medical Device Applications

Bones consist of two different tissue formations: cancellous (trabecular) bone and cortical bone. Cancellous tissue has a porosity of 70 - 90% by volume, while cortical tissue is the dense bone layer with a porosity of under 10% by volume. Both types of bone tissue experience dynamic remodeling, maturation, differentiation, and resorption processes regulated by interactions between bone cells [110]. When bone damage occurs in any part of the body and is too large to heal with the remaining bone tissue, implants are required. The preparation of scaffolds and the production of implants by adjusting the pore size using 3D printing is considered the most advanced method for repairing such damages. Due to the different anatomical structures of each patient and the possibility of having various levels of defects, personalized production and treatments can be achieved with the design and production flexibility of 3D printing technology [101].

Implants must exhibit good biocompatibility and flexibility structurally, provide the necessary pore size and porosity, and have appropriate mechanical properties. SSs, Ti and Ti alloys, and Co-Cr alloys are frequently used as implant materials.

Because of their outstanding biocompatibility, high corrosion resistance, and high osseointegration (implant-bone compatibility) characteristics, Ti and Ti alloys (especially Ti6AL4V) have long been the most preferred implant materials [111, 112]. The structure of the pores and porosity facilitate cell adhesion and support the transfer of substances (oxygen, nutrients, etc.) to the implant, promoting bone growth, development, and renewal [113]. In addition to providing the desired porosity, the implant must also have good mechanical strength [114]. Soro et al. [115] produced structures with three different pore structures using SLM technology with Ti6Al4V material and investigated the mechanical characteristics of these structures for hard tissue implant

applications. Bai et al. [103] examined the design processes and methods of metal implants in detail, addressing various features of lattice structures based on topological optimization in implant scaffolds. It was emphasized that producing these designs with complex structures using PBF technology provides significant flexibility for the design-manufacturing process. The greatest widely utilized AM technology for the creation of hard bone tissue implants is LPF applications [116].

Numerous bone implants, such as cranial [117, 118], hip [119], shoulder [120], and thoracic cage implants [121], are personalized and produced as needed using AM technology. Fig. 4 illustrates the production process flow of a cranial implant, beginning with medical imaging and culminating in final processing via SLM technology [117]. The procedure generally starts with the transmission of the patient's radiological images (such as Magnetic Resonance Imaging/Computed Tomography) to the relevant center. Radiological images are digitally transmitted using special programs (DICOM - Digital Imaging and Communications in Medicine). The images are converted from 2D to 3D models using programs such as MIMICS, and the design of the appropriate part is carried out by specialists using various software (3-matic). The 3D damaged model and the suitable part for the model are initially produced with plastic material, and then, with the physician's approval, the Ti part is produced. The implants must be sterilized before the clinical operation. During the operation, after the necessary treatment for the patient (such as tumor removal) is performed, the sterile implant is placed in the damaged area [117, 118].

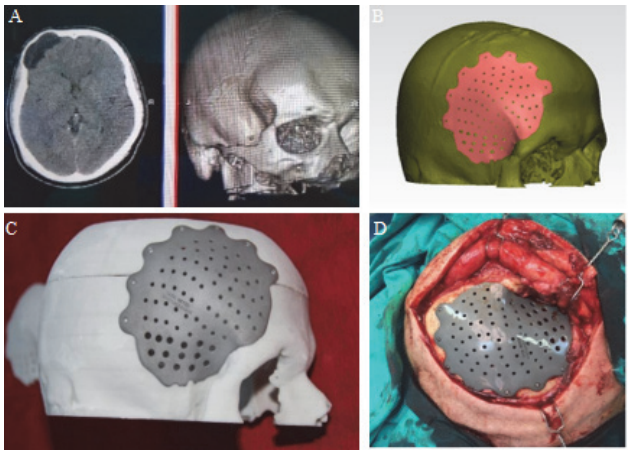

Figure 4 General process flow for the production of implants using 3D printing [117]

Bartolomeu et al.[119] produced hip implants using NiTi and Ti6Al4V materials with the SLM method. The aim was to minimize the need for revision surgeries by producing implants with optimal properties using NiTi and Ti6Al4V materials. The shape memory capability of the NiTi alloy was used for controlled volume expansion, while the Ti6Al4V alloy provided the desired hardness and mechanical strength. As a result, it was observed that implants could be produced using multiple materials like this to achieve the desired osseointegration and support inward bone growth. However, further development of these findings is needed.

Beliën et al. [120] created a new treatment method utilizing a 3D model and patient-specific restoration plates to manage acromial (shoulder bone) fractures. This treatment method was applied to five patients, and the results were reported. The study confirmed that this treatment method is a highly suitable solution for patients who have not previously undergone long medical treatment.

Goldsmith et al. [121] produced a thoracic cage implant using Ti alloy powders with SLM technology. A digital 3D model was created by performing scanning and segmentation on the area of the tumor that occurred in the middle of the patient's thoracic cage. The damaged area was printed using SLA technology for surgical planning. An implant was produced from Ti alloy powders (TiMG1) using the SLM method, sterilized before the surgery, and appropriately implanted into the patient's body after tumor removal. After implantation, the patient was regularly monitored with respiratory tests and physiotherapy exercises. No adverse events occurred, and the treatment was successful.

Yang et al. [122] compared irregular pore structure bone scaffolds and the previously accepted regular cubic pore scaffolds using Voronoi-structured trabecular-like scaffold (VBTS) designs for trabecular bone implants. Using Ti6Al4V material, one regular cubic scaffold and three VBTS with varying pore sizes were manufactured using EBM technology. The mechanical performance, biocompatibility, osteogenic differentiation, and bone regeneration features of the four types of scaffolds were appraised using in vitro and in vivo test outcomes. It was determined that the mechanical features were within the range of human bone structure, VBTS provided good biocompatibility, and showed positive results for osteogenic differentiation. Additionally, it was determined that the VBTS featuring a mean pore size of 596 μm was the best suitable pore size for bone regeneration and cell proliferation (Fig. 5).

AM is also an effective method for the production of many medical devices and therapeutic equipment. Polymer materials are commonly utilized in the fabrication of these medical instruments. The material selection and appropriate 3D printing technique are determined by analyzing the properties of the part to be produced, such as flexibility, hardness, density, temperature response, durability, and compressibility. In addition to FDM and SLA, the SLS technique is also among the best preferred 3D printing techniques in this field [102]. 3D printing techniques enable the personalization of medical devices and equipment such as orthotics and prosthetics that fit the patient's anatomy [123], surgical guides [124], hearing aids [59], and glasses [125], providing many options for patient treatment.

Fig. 6 shows the creation of individualized glasses designed according to the patient's anatomy and manufactured using 3D printing technology. In the study, an innovative new method for producing custom glasses using SLA technology was presented for a child patient with facial deformity due to Goldenhar syndrome [125].

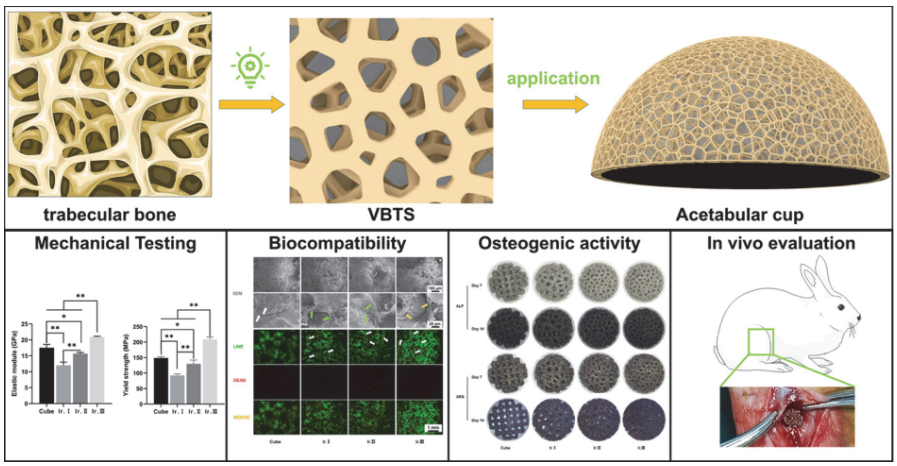

Figure 5 Voronoi-structured trabecular-like scaffold (VBTS) structure, application example, and schematic summary of the tests performed [122]

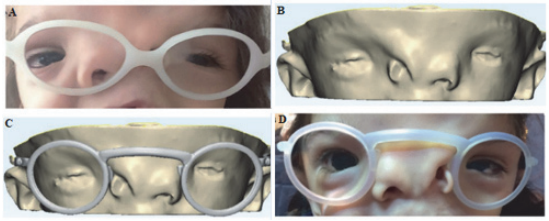

Figure 6 3D design of the child's midface software data and glasses. (A) Wearing a standard pair of glasses before 3D printing technique. (B) The anatomical 3D solid model of the midface is digitally created by a special software program. (C) The glasses are digitally positioned on the face with optical alignment. (D) Ensuring that the glasses produced by 3D printing fit the patient's face appropriately [125].

Banga et al. [126] produced a custom ankle orthosis for children using AM technology. Instead of polypropylene used in standard ankle orthoses, carbon fiber material was used to produce the orthosis utilizing the FDM technique. It was noted that when carbon fiber was used, the produced orthosis showed greater durability against stress, improving mechanical strength and alleviating patient defects.

5 RESULTS AND EXPECTATIONS

AM applications provide advantages aimed at improving treatment processes and methods in the medical sector. The results obtained from this study are summarized below:

- Different tissue and organ defects can be repaired by creating scaffolds using 3D bioprinting techniques. Organs produced by 3D bioprinting can be applied in various drug tests or disease modeling.
- Surgical modeling, which exhibits characteristics such as mechanical strength, hardness, and flexibility equal to living tissues, is performed using multiple materials for surgeries involving complex anatomical structures.
- Anatomical surgical models provide surgeons with preoperative planning opportunities. The surgeon becomes familiar with the patient's anatomical structure from all angles and minimizes potential complications during the operation. This results in shorter surgery times and increased success rates.
- Custom-designed and produced implants and medical devices can be created. The structure, shape, pore size, and porosity of the implants are specifically designed and produced to optimally promote inward bone growth and osseointegration.

Expectations regarding various medical applications using AM methods are increasing day by day. Therefore, further development is needed [127]. There is a need to increase the diversity of biomaterials. four-dimensional (4D) printing technology has emerged by incorporating the element of time into 3D printing. 4D bioprinting scaffolds must react to environmental cues such as hormones, cells, temperature, pH, and pressure [128, 129]. As a result of developing the 4D bioprinting technique alongside various biomaterials, it is expected that the artificial organs produced will react to body reactions like natural organs and change size over time according to the development of the organism. This will significantly reduce the need for organ transplants.

6 CONCLUSION

This review provides a comprehensive and up-to-date overview of AM technologies and their medical applications, highlighting their increasing relevance in personalized healthcare. What sets this review apart from previous studies is its integrative approach that not only categorizes AM materials and techniques, but also systematically connects them to specific medical applications such as tissue engineering, organ modeling, and implant development. Unlike earlier reviews that often focused narrowly on either materials or technology, this study bridges the gap between both dimensions.

Furthermore, the inclusion of detailed application cases-such as mandibular tissue regeneration, cranial implant manufacturing workflows, and thoracic cage reconstructions-offers practical insights that reinforce theoretical knowledge. This review also distinguishes itself by presenting a clear comparative analysis of AM methods with their functional outputs, enabling a deeper understanding of how material choices align with desired clinical outcomes.

Additionally, the novelty of this work lies in its forward-looking discussion on the integration of 4D printing in the medical field. By introducing concepts such as smart biomaterials and environmentally responsive scaffolds, the review contributes to future directions in regenerative medicine and organ replacement technologies. As a result, this work not only synthesizes

existing knowledge but also suggests a roadmap for future innovations, making it a valuable resource for researchers, engineers, and clinicians working at the intersection of biomedical engineering and advanced manufacturing.

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